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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/932,227 09/17/97 FOSSEL

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EXAMINER

IM52/0725

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BOSTON MA 02109

MULLIS, T	
ART UNIT	PAPER NUMBER

1711
DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Applicati n No.

08/932,227

Applicant(s)

FOSSEL, ERIC T.

Examiner

Jeffrey C. Mullis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-35,38-44,47-53,56-59 and 61-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-35,38-44,47-53,56-59 and 61-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 14) ☐ Notice of References Cited (PTO-892)
- 15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 17) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 18) ☐ Notice of Informal Patent Application (PTO-152)
- 19) ☐ Other: _____

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All remaining rejections and/or objections follow.

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "L-arginine ethyl", "L-arginine methyl", "L-arginine propyl", "L-arginine butyl", "L-arginine isobutyl", and "L-arginine t-butyl" are not art recognized and are therefore unclear. If these are intended to be esters, i.e. methyl, propyl, etc. ester, then applicant is being redundant since these esters are already mentioned in the claims. In any case, it is unclear where these alkyl moieties such as methyl are present on the arginine molecule except with regard to those specific species which specifically recite "ester".

Applicant remarks that the claims have been amended and that "the instant invention now does not claim L-arginine, only the specific derivatives" in Section IV of his remarks is not understood since this statement can be variously interpreted as referring to derivatives of the materials recited by the claims or may mean that the "specific derivatives" are in fact the specific species (and not their derivatives) of L-arginine specifically now recited, i.e. for instance "L-arginine ethyl ester" being the actual species referred to, i.e. a derivative of arginine and not a derivative of L-arginine ethyl ester.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 33-34, 38, 51-53 and 59 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weuffen et al. (USP 5,629,002).

See the Office action of Paper No. 6 at page 4 lines 5 et seq.

Claim 33 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hechtman (USP 5,595,753).

See the Office action of Paper No. 6 at the paragraph bridging pages 4 and 5 et seq.

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Claims 61-63 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Garfield et al. in view of Hechtman, Altadonna (USP 5,853,768), Cooke et al. (USP 5,428,070), Saavedra et al. (USP 5,632,981) and Cooper et al.

See the Office action of Paper No. 8 at the paragraph bridging pages 3 and 4 et seq.

Applicant's arguments filed 5-1-01 have been fully considered but they are not deemed to be persuasive.

With regard to Weuffen, applicant argues that the Examiner is reading teachings into this reference that are not there. While it is true that certain explicit teachings are not present in Weuffen which are required by the claims, it is applicant's burden to prove that a characteristic is not present where all other limitations of the claims are present. Applicant argues that he does not now claim L-arginine. While it may be true that applicant's claims no longer embrace L-arginine in underivatized form, the arginine in Weuffen is present with glutamic acid as well as chloride and therefore the L-arginine of Weuffen is present as a glutamic acid salt or chloride salt.

With regard to the 35 U.S.C. § 103(a) portion of the rejection over Weuffen, the Weuffen patent teaches a specific method for increasing hair growth through the use of increased blood flow. However applicant's own claims specifically recite a "method of increasing localized blood flow". Propyl nicotinate

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and sodium thiocyanate potentiation of this effect is in no way excluded by the claims. The instant claims do not exclude any additional materials disclosed by the reference.

With regard to Hechtman, applicant argues that Hechtman discloses the use of N⁶-nitro-L-arginine methyl ester. However applicant has not been entirely clear as to whether they consider this species embraced by his claims. Applicant's statement that the "claims have been amended and the instant invention now does not claim L-arginine, only the specific derivatives" is not understood. This argument of applicant might possibly be interpreted as meaning that applicant is claiming derivatives of the materials explicitly recited by the claims. Alternatively applicant may be arguing that the only arginine species being claimed are those specific species recited explicitly by the claims, not derivatives of those species. **If so, the Examiner agrees that Hechtman does not render the claims obvious or anticipated.** Furthermore, some of the species recited above are unclear in and of themselves as set out in the above rejection under 35 U.S.C. § 112 second paragraph. Again with regard to applicant's characteristics, these are assumed to be inherent given that all other features of the reference are disclosed. Applicant has of course argued that different compounds are present in Hechtman and Weuffen but as set out above, the

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Examiner does not agree that the claims clearly require the compounds not disclosed by the two references. Applicant argues that the method of claims 33 and 34 is directed to different use than that of the prior art but the only use recited in these claims is a method of increasing blood flow and increasing growth rates. However increased growth rates and blood flow for repair of cells appears to result from topical application of a specific composition. Since the prior art and the claims appear to embrace topical application of the same composition applicant's increased growth rate and blood flow characteristics appear to be inherent.

With regard to the rejection under 35 U.S.C. § 103 relying upon Garfield et al. as the primary reference, applicants argue that the background of Garfield et al. states that "Stimulated macrophages produce nitric oxide from L-arginine and it is considered the first line of defense against invading pathogens". However the Examiner cannot find the specific quotation in the reference. Applicant argues that the reference then continues with a list of NO donors in Table 1 in which L-arginine is present. However it is not clear whether applicant intends that substitution of for instance L-arginine esters are included in their definition of their arginine species. As set out above, clarification is required.

Applicant appears to argue that Garfield does not teach any of the treatments required by the claims. However, Garfield

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discloses explicitly the healing of wounds which is embraced by applicants' repair of cells. Applicants argue that the claims have been amended to remove the NO donor reference. However it is immaterial if the propriety of the rejection whether or not the NO donor reference is present in the claims. Since the references clearly disclose nitric oxide donation and since the claims do not exclude nitric oxide donation ability there is motivation to make the proposed modifications. Since the primary reference requires a nitric oxide donor and since the secondary reference discloses such substances which are particularly safe in comparison to other nitric oxide donators, there is ample motivation to combine Hechtman with the primary reference.

With regard to Cooke '070, the primary reference teaches topical application and it is therefore unnecessary that the secondary reference teaches such. Application to the skin suits the purposes of the primary reference and therefore there is motivation to use topical application based on the teachings of the primary reference.

With regard to Altadonna '768, the Examiner agrees that claims 33, 42 and 51 require salts that are not present or suggested by the combination of references. However claim 61 is not limited as to any particular salts.

With regard to Saavedra '981, it is not the position of the Examiner that Saavedra necessarily teaches topical use of L-

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arginine but rather does teach the use of topical application of a nitric oxide releasing substance to treat impotence. It is the primary reference which (arguably as set out above in the above rejection under 35 U.S.C. § 112 second paragraph), teaches applicant's specific arginine substances.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Jeffrey Mullis at telephone number (703) 308-2820.

J. Mullis:cdc

July 17, 2001

Jeffrey Mullis
Primary Examiner
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